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Lysyl oxidase: A versatile and elusive enzyme

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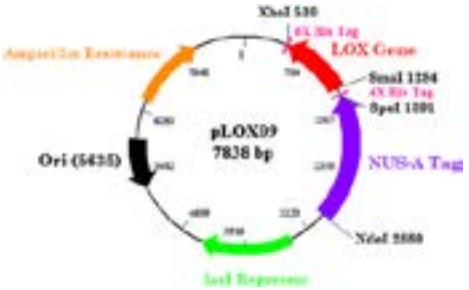
Lysyl oxidase is an extracellular matrix, copper-dependent, amine oxidase that catalyzes a key crosslinking step in collagen and elastin. The enzyme is synthesized as a proenzyme that, upon excretion to the extracellular matrix, is cleaved at the Gly168-Asp169 bond by procollagen C-proteinase in the mammalian form of the enzyme. Lysyl oxidase is highly regulated and changes in its regulation have been shown to play a role in fibrosis and several other diseases. More recently, the enzyme has been shown to play a paradoxical role in cancer. In the early stages of cancer, the cleaved pro-peptide has been shown to inhibit the RAS oncogene, whereas in late stages of cancer lysyl oxidase has been shown to promote metastasis. Lysyl oxidase is highly insoluble and this has hampered its full characterization. Recent work in the by our study group has addressed some of the issues associated with the insolubility and characterization of the enzyme. In particular, this talk will address how plasmids were used to increase enzyme yields over those obtained directly from bovine aortic tissue, the role solubility tags play on enzyme activity and suitability for characterization studies, and will end with an innovative new approach to drug delivery that targets lysyl oxidase in cancer cells but remains inactive in normal cells.



Recent Publications

1. Oldfield R, Johnston K, Limones J, Ghilarducci C and Lopez K (2017) Identification of histidine 303 as the catalytic base of lysyl oxidase via site – directed mutagenesis. The Protein Journal, doi: 10.1007/s10930-017-9749-3.
2. Smith M A, Gonzalez J, Hussain A, Oldfield R N, Johnston K A, et al. (2016) Overexpression of soluble recombinant human lysyl oxidase by using solubility tags: effects on activity and solubility. Enzyme Research 2016:1-7.
3. Lopez K and Greenaway F T (2011) Identification of the copper-binding ligands of lysyl oxidase. Journal of Neural Transmission 118:1101-1109.
4. Herwald S, Greenaway F and Lopez K (2010) Purification of high yields of catalytically active lysyl oxidase directly from Escherichia coli cell culture. Protein Expression and Purification 74:116-121.

Biography

Karlo M Lopez is currently an Associate Professor of Biochemistry at California State University, Bakersfield. He received a PhD from Clark University and was a Howard Medical Institute Fellow at Pomona College. His research focuses primarily on the structural characterization of lysyl oxidase and understanding the role this enzyme plays in cancer metastasis. He is a member of the Committee on Ethics of the American Chemical Society and was part of the Task Force for Safety Education Guidelines.

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